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## NOTICE OF ALLOWANCE AND FEE(S) DUE

25908 7590 12/16/2008

NOVOZYMES NORTH AMERICA, INC.  
500 FIFTH AVENUE  
SUITE 1600  
NEW YORK, NY 10110

EXAMINER

MOORE, WILLIAM W

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 12/16/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/807,096

03/22/2004

Allan Svendsen

10321.200-US

2911

TITLE OF INVENTION: SUBTILASES

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1510	\$300	\$0	\$1810	03/16/2009

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.**

**THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.**

### HOW TO REPLY TO THIS NOTICE:

#### I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.**

# **PART B - FEE(S) TRANSMITTAL**

**Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE  
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

25908 7590 12/16/2008

**NOVOZYMES NORTH AMERICA, INC.**  
500 FIFTH AVENUE  
SUITE 1600  
NEW YORK, NY 10110

## **Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,096	03/22/2004	Allan Svendsen	10321.200-US	2911

TITLE OF INVENTION: SUBTILASES

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1510	\$300	\$0	\$1810	03/16/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
MOORE, WILLIAM W	1656	435-219000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 \_\_\_\_\_
- (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 \_\_\_\_\_
- 3 \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies \_\_\_\_\_

4b. Payment of Fee(s); (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

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Date \_\_\_\_\_

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This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,096	03/22/2004	Allan Svendsen	10321.200-US	2911
25908	7590	12/16/2008	EXAMINER	
NOVOZYMES NORTH AMERICA, INC. 500 FIFTH AVENUE SUITE 1600 NEW YORK, NY 10110			MOORE, WILLIAM W	
			ART UNIT	PAPER NUMBER
			1656	
DATE MAILED: 12/16/2008				

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 501 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 501 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

<b>Notice of Allowability</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/807,096	SVENDSEN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	WILLIAM W. MOORE	1656	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the amendments filed 4 September 2008 and the interview conducted 10 December 20008.

2. ☒ The allowed claim(s) is/are 56,59 and 61-65.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some\* c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.

3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.

(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached

1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_.

(b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_.

**Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)

2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3. ☐ Information Disclosure Statements (PTO/SB/08),  
Paper No./Mail Date \_\_\_\_

4. ☐ Examiner's Comment Regarding Requirement for Deposit  
of Biological Material

5. ☐ Notice of Informal Patent Application

6. ☐ Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_.

7. ☒ Examiner's Amendment/Comment

8. ☒ Examiner's Statement of Reasons for Allowance

9. ☐ Other \_\_\_\_.

/William W. Moore/  
10 December 2008

/Rebecca E. Prouty/  
Primary Examiner  
Art Unit 1652

## EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee. All allowed claims, whether amended or not, are included to aid the printer.

The application has been amended as follows:

Cancel claims 40-55 and 60.

Amend claims 56, 59 and 61-65 thus:

Claim 56. (Currently amended) A variant of a JP170 type subtilase, said variant having at least 95% identity to SEQ ID NO:1 and comprising at least one amino acid sequence modification in an amino acid residue in at least one position of an ion-binding site 1, an ion-binding site 2, or an ion-binding site 3, or combinations thereof, wherein the at least one position of ion-binding site 1 is selected from the group of positions consisting of 183, 184, 185, 186, 187, 188, 189, 191, 196, 197, 198, 199, 200, 201, 202, 203, 224, 225, and combinations thereof; wherein the at least one position of ion-binding site 2 is selected from the group of positions consisting of 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, and combinations thereof; and wherein the at least one position of ion-binding site 3 is selected from the group of positions consisting of 348, 350, 352, 363, 364, 365, 366, 367, 370, 394, 395, 396, 397, 398, 399, 400, 414, 415, 416, 417, 418, 419, 420, and combinations thereof; and wherein the numbering of said positions corresponds ~~correspond~~ to the amino acid positions of SEQ ID NO:1.

Claim 59. (Currently amended) A variant of a JP170 type subtilase, said variant having at least 95% identity to SEQ ID NO:1 and comprising at least one amino acid sequence modification in a mobile or highly mobile region of the subtilase, wherein the modification is at ~~in~~ a position selected from the group consisting of: 13, 14, 15, 16, 17, 18, 37, 38, 39, 40, 41, 42, 43, 47, 48, 49, 50, 58, 59, 60, 67, 96, 97, 98, 99, 108, 109, 110, 111, 131, 132, 133, 134, 152, 153, 163, 164, 165, 166, 188, 189, 190, 191, 210, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 326, 327, 328, 329, 330, 331, 332, 337, 338, 339, 340, 355, 356, 357, 359, 360, 372, 373, 374, 375, 376, 377, 378, 384, 385, 387, 388, 389, 390, 391, 392, 404, 405, 406, 407, 408, 409, 410, 411 and

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419, ~~wherein the subtilase has at least 95% similarity to SEQ ID NO:1, and wherein the~~  
numbering of said positions corresponds ~~correspond~~ to the amino acid positions of SEQ ID  
NO:1.

Claim 61 (Currently amended) The variant of claim 56, wherein the at least one amino acid  
sequence modification comprises at least one of the substitutions ~~modifications~~: D196N;  
H200D; H200N; ~~H200D, N~~; N390D; N391D; W392S; W392N; W392Q; ~~W392S, N, Q~~; and  
G394N; G394Q; G394F; G394Y; and G394S; ~~G394N, Q, F, Y, S~~.

Claim 62 (Currently amended) A variant of a JP170 type subtilase having at least 95% identity  
~~similarity~~ to SEQ ID NO:1 comprising the introduction of an ion-binding site corresponding  
to the Strong ion-binding site of the BPN' like family subtilases, wherein said variant has a  
partial or full deletion of the region corresponding to the amino acid positions N79-N82 of  
SEQ ID NO:1 and a subsequent insertion of one or more amino acid residues in the same  
location, and wherein said positions correspond to the amino acid positions of SEQ ID  
NO:1.

Claim 63 (Currently amended) The variant of claim 62, wherein the sequence LNNSIQV set  
forth in SEQ ID NO:5 ~~(SEQ ID NO:5)~~ is inserted; and the variant further comprises either of  
~~followed by~~ the substitutions A45D or A45N, wherein said position 45 corresponds to the  
position 45 of SEQ ID NO:1 ~~substitution A45D, N~~.

Claim 64 (Currently amended) The variant of claim 56, wherein the at least one amino acid  
sequence modification comprises either the pair of substitutions H200D+D196N or the pair  
of substitutions H200N+D196N.

Claim 65 (Currently amended) The variant of claim 63, further comprising at least one of the  
substitutions ~~modifications~~: E44P, E44T, ~~E44P, T~~ and R47Q.

Authorization for this examiner's amendment was given in a telephone interview with Ms.  
Kristin McNamara on 10 December 2008.

The following is an examiner's statement of reasons for allowance:

Applicant's amendment filed 4 September 2008 removes the bases for the objection of  
record of claim 63 herein and the rejections of record of claims 56, 57, and 59-63, herein under  
the first and second paragraphs of 35 USC § 112, and under 35 USC § 102. Applicant's  
arguments are persuasive in overcoming the rejection of record of claims 56 and 59-61 under  
35 USC § 103(a) because one of ordinary skill in the art would not have been able to determine  
whether or not an amino acid might contribute to the formation of a calcium binding site, or  
reside at the surface of a polypeptide, thus be a worthwhile selection for an amino acid

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substitution taught by Zukowski et al., unless and until a determination of the three-dimensional structure of a JP170 had been made. While three-dimensional structures for many smaller, standard, monodomain subtilisins were previously determined, e.g. subtilisin BPN in 1984 (2.6Å resolution), which is SEQ ID NO:4 herein compared in Figure 4, and subtilisin 309 in 1992 (1.4Å resolution), which is SEQ ID NO:8 herein compared in Figure 4, only the amino acid sequence of JP170 had earlier been determined. Although the catalytic domain region of JP170 might be identifiable on the basis of sequence alignment, additional insertions within this region relative to those of smaller monodomain subtilisins, and the carboxyl-terminal 115 amino acids that have no relationship to the sequences of subtilisins whose structures had been determined, required the resolution by the co-inventors herein of JP170's three-dimensional structure to identify positions might be solvent-accessible, identify those that may interact with amino acids in other positions, and to identify those within mobile regions and/or ion-binding regions which might therefore be available for individual amino acid substitutions or multiple amino acid sequence position replacement(s). The examiner's amendment resolves the remaining prior art issues in favor of allowance of claims 56, 59, and 61-65, and also clarifies the recitations of these claims by indicating that a subtilase variant amino acid sequence sharing at least 95% sequence identity with the amino acid sequence set forth in SEQ ID NO:1 is modified according to disclosures at, *inter alia*, page 8 of the specification. Claims 62 and 63 are further amended to better reflect disclosures at pages 19 and 32 of the specification.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Jon Weber, Ph.D., can be reached at 571.272.0925. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or

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relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/William W. Moore/  
10 December 2008

/Rebecca E. Prouty/  
Primary Examiner  
Art Unit 1652